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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/988,835	11/19/2001	Gideon Strassmann	MTN-031CN	9376

959 7590 09/08/2003

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BOSTON, MA 02109

EXAMINER
WINKLER, ULRIKE

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 09/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/988,835	STRASSMANN ET AL.	
	Examiner	Art Unit	
	Ulrike Winkler	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-11 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-11 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-11 are pending in this application and claims 1-11 are rejected.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: The signature of an inventor is missing. Acknowledgment is hereby made of the applicants' petition under 37 CFR 1.47 (a). The petition will be forwarded to the Special Programs Law Office.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5-8 and 11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification shows that in a GDF-8 knock-out-mouse the expression of GLUT-4 is increased in all muscles cells (see example 1). The specification additionally shows that administration of GDF-8 causes weight loss and a significant decrease in the levels of GLUT-4 expression in muscle cells (see experiment 2).

The claims encompass methods using a genus of compounds defined only by their function (inhibitor of GDF-8) wherein the relationship between the structural features of

members of the genus and said function have not been defined. In the absence of such a relationship either disclosed in the as filed application or which would have been recognized based upon information readily available to one skilled in the art, the skilled artisan would not know how to make and use compounds that lack structural definition. The fact that one could assay a compound of interest using the claimed assays does not overcome this defect since one would have no knowledge beforehand as to whether or not any given compound (other antibodies directed to GDF-8) would fall within the scope of what is claimed. It would require undue experimentation (be an undue burden) to randomly screen undefined compounds for the claimed activity.

Although the description does not provide working examples, the description teaches a method for measuring the biochemical the expression of GLUT-4 in tissue and the person skilled in the art can understand how to use the screening method considering the common general knowledge.

To comply with the written description requirement of 35 U.S.C. § 112, first paragraph, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was ready for patenting" such as by the use of drawings or structural chemical formulas that show that the invention was complete, or

describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention.

The claimed invention is drawn to methods of increasing the expression of GLUT4 or a method of increasing insulin sensitivity in a subject by administering a GDF-8 inhibitor. However, no structural or specific functional characteristics of such an peptide fragment inhibitors, GDF-8 receptor agonist, dominant negative mutant GDF-8, a non-GDF-8 peptide, antisense, ribozyme inhibitors and an inhibitor that is derived from the Pro-GDF-8 domain is provided. This situation is analogous to that of *Regents of the University of California v Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). Because one skilled in the art would conclude that the inventors were not in possession of the claimed invention. The claim fails to comply with the written description requirement.

Claims 1-3, 5-8 and 11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification shows that in a GDF-8 knock-out-mouse the expression of GLUT-4 is increased in all muscles cells (see example 1). The specification additionally shows that administration of GDF-8 causes weight loss and a significant decrease in the levels of GLUT-4 expression in muscle cells (see experiment 2). The specification does not disclose the GDF-8 receptor or a peptide fragment inhibitors, GDF-8 receptor agonist, dominant negative mutant GDF-8, a non-GDF-8 peptide, antisense, ribozyme inhibitors and an inhibitor that is derived from the Pro-GDF-8 domain.

To comply with the enablement requirement of 35 U.S.C. § 112, first paragraph, the specification must enable one skilled in the art to make and use the claimed invention without undue experimentation. The claims are evaluated for enablement based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows: (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims. Such an analysis does not need to specifically enumerate (points 1-8) but only needs to have a select few of the factors present discussed in a rejection.

The specification shows that in a GDF-8 knock-out-mouse the expression of GLUT-4 is increased in all muscles cells (see example 1). The specification additionally shows that administration of GDF-8 causes weight loss and a significant decrease in the levels of GLUT-4 expression in muscle cells (see experiment 2). The specification does not reasonably provide enablement for peptide fragment inhibitors, GDF-8 receptor agonist, dominant negative mutant GDF-8, a non-GDF-8 peptide, antisense, ribozyme inhibitors and an inhibitor that is derived from the Pro-GDF-8 domain. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The applicant has not provided any biochemical data such as molecular weight and amino acid composition of the peptide inhibitors. The applicant also does not disclose what biochemical features a non-GDF-8 peptide inhibitor encompasses. The specification neither teaches the GDF-8 receptor nor making a receptor agonist. The

specification does not disclose the structure of the GDF-8 receptor, the knowledge would be required to envision antagonist that may bind to this receptor, knowledge of the receptor structure is required in order to test whether peptide fragment inhibitors are involved in the GDF-8 mediated effects. The specification does not teach how to make and use the claimed inhibitors; without such guidance the applicant is inviting the artisan to engage in undue experimentation.

The claims meet the utility requirement of 35 U.S.C. § 101. Only one specific, substantial, and credible utility is required to support the requirements of 35 U.S.C. § 101. In the instant case the presence the specification has shown a correlation between GDF-8 and the GLUT-4 receptor which is a hexose transporter. The specification provides prophetic examples in how an artisan might go about making such inhibitors and suggests assays that might be useful to do this. The specification does not set forth sufficient teachings to allow one skilled in the art to use any compound besides an anti-GDF-8 antibody. Using inhibitors such as dominant negative mutant of GDF-8, a GDF-8 receptor agonist, a non-GDF-8 peptide, an antisense nucleic acid or ribozyme is unpredictable in the dynamic physiological setting of a subject. The specification provides insufficient guidance with regard to theses issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict the efficacy of the claimed method of treatment and composition with a reasonable expectation of success in regards to using a dominant negative mutant of GDF-8, a GDF-8 receptor agonist, a non-GDF-8 peptide, an antisense nucleic acid or ribozyme. Moreover, the nature of the invention and the state of prior art have not provided any reasonable expectation of success especially in regards to antisense nucleic acid or ribozyme inhibitors in the context of a subject. For the above reasons, it appears

that undue experimentation would be required to practice the claimed invention with a reasonable expectation of success.

The instant fact pattern fails to disclose any particular structure for the claimed inhibitors. The specification does not provide any guidance or any working examples in this unpredictable art, and thus the artisan would have been unable to have prepared the claimed GDF-8 inhibitor without undue experimentation. Treatment/administration protocols depend upon the nature of the compound being administered as well as the clinical condition of the subject or patient. In the absence of additional information the skilled artisan would not have been able to use the undisclosed compound(s) for treatment without undue experimentation.

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 4, 9, 10 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-7 of prior U.S. Patent No. 6,368,597. This is a double patenting rejection.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3, 5-8 and 11 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1-7 of U.S. Patent No. 6,368,597. Although the conflicting claims are not identical, they are not patentably distinct from each other because the patented claims are drawn to treatment methods with an antibody inhibitor.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 703-308-8294. The examiner can normally be reached M-F, 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 703-308-4027.

The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for informal communications use 703-308-4426.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

ULRIKE WINKLER, PHD.
PATENT EXAMINER
9/5/03